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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,708	04/05/1999	GWENYTH JANE FARRAR	MUR-7520	9036

44966 7590 10/20/2004

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/155,708	FARRAR ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13,16-21,25-27,32-37,41-52 and 54-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,13,16-21,25-27,32-37,41-52 and 54-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 4-5-99 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-15-03; 8-26-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *5-27-04*.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The Office Action mailed 12-04-2003 was intended to be a Non-Final Rejection and not a Final Rejection as indicated on the Office Action Summary (PTO-326) mailed 12-04-2003. Therefore, the Request for Continued Examination (RCE) filed 5-27-2004 was improper as per 37 CRF § 1.114, since prosecution in the instant case was not closed prior to the filing of the RCE.

3. The Substitute Specification filed 7-13-2001 was considered proper and was entered by the Examiner.

4. Applicants are reminded that the drawings submitted 4-05-1999 were objected to by the Draftsperson as set forth in the Notice of Formal Drawings Required attached to the Office Action mailed 2-13-01.

Response to Arguments

Claim Rejections - 35 USC § 102

5. Claims 12-13, 16-21, 26, 32-37 and 42-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Roth et al. (US Patent No. 6,482,803; see entire document), for the reasons of record set forth in the Official Action mailed 2-27-03.

6. This rejection was improperly withdrawn in the Office Action mailed 12-04-03. Applicant's Arguments filed 9-17-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that Roth et al. does not teach each and every aspect of the instant invention. In particular, Applicants argue that Roth et al. teaches

away from the instant invention, to the extent that the ribozymes of Roth et al. are not designed to target a coding region of a mature mRNA. Applicants cite column 3, lines 1-16, to support their position. However, contrary to Applicant's assertions, it is noted that the invention of Roth et al. is not limited to wherein the ribozymes (i.e. the suppression effector) are limited to only cleaving pre-mRNA. In another embodiment of the Roth et al. invention, it is broadly contemplated that the method include wherein the ribozymes targets the mutant p53 mRNA and clearly distinguishes between p53 mRNA and native p53 pre-mRNA. See for example, col. 7, lines 9-14, which state "[T]he ribozymes of the present invention have been developed to selectively modify p53 mRNA. For example, ribozymes are designed to target a specific mutated codon in p53 mRNA for cleavage. ***Alternatively***, ribozymes of the present invention targeted to "native" sequences such as intron-exon splice sites of pre-mRNA that can be genetically engineered out of other, compensatory constructs (see col. 7, lines 9-14)." Therefore, contrary to Applicant's assertions, the disclosure of Roth et al. encompasses Applicant's claimed invention, wherein the suppression effector is a nucleic acid and wherein the ribozyme targets a codon in the coding sequence of a mature RNA.

Claim Rejections - 35 USC § 112

7. Claims 12, 25, 41-44, 51, 62-64, 70-71, 73, and 75-77 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 2-27-03.

8. Applicant's arguments file 3-08-04 have been fully considered, but they are not persuasive. Applicants traverse the instant rejection by way of amending the instant claims to recite wherein the suppression effector is a nucleic acid or a peptide nucleic acid (PNA). However, independent claims 12, 44 and 51, as amended encompass wherein the replacement nucleic acid encodes a wild-type or non-disease causing allele that comprises a single nucleotide difference in comparison to the mutant allele. However, other than ribozyme suppressors Applicant's have not provided any evidence that an antisense nucleic acid or peptide nucleic acid could be used to specifically target a mutant allele and not suppress the wild-type allele that differs only by a single nucleotide. Absent evidence to the contrary, due to the nature of antisense and PNA, it is not required that either the antisense or PNA be 100% complementary to an mRNA sequence in order to effectively reduce the activity of the mRNA sequence. Furthermore, absent evidence to the contrary an antisense oligonucleotide or PNA would also reduce the expression of a replacement nucleic acid comprising a single nucleotide change at a degenerate or wobble site in a nucleic acid.

Moreover, due to the lack of description in the specification as filed, it is unclear how one of skill in the art would be able to predict the structures of antisense or PNA and/or other forms of suppression effectors (such as siRNA), which possesses the required functionality as set forth in the instant claims. One of skill in the art would have to resort to trial and error experimentation in order to identify the full scope of compounds encompassed by the claimed invention. In light of the fact that further experimentation is required to identify the full scope of compounds that are useful in the claimed methods and kits, it is apparent that full scope of the claimed invention was not reduced to practice at the time of filing of the claimed invention.

Therefore, the full scope of the claimed invention was not "ready for patenting" at the time of filing of the present invention.

9. Claims 46-49 and 65-67 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the Office Action mailed 12-04-03.

Applicant's arguments file 3-08-04 have been fully considered, but they are not persuasive. Applicants traverse the instant rejection by way of amending the instant claims to recite "a nucleotide sequence encoded by." However, to the extent that the term "nucleotide" may encompass both ribonucleotides and deoxynucleotides, Applicant's amendment does not make it clear that the encoded sequences is a ribonucleotide, the instant claims remain rejected for the reasons of record. As stated previously, it is well known in the art that ribozymes require the presence of the 2'-OH hydroxyl in the ribose sugar for catalysis of RNA cleavage, see for example Figure 1, page 1146 of Takagi et al. (2002), and Burke (2002) 1st ¶, page 1118. Applicant's must amend the instant claims to recite wherein the encoded nucleotides are ribonucleotides, since the term nucleotide also encompasses deoxynucleotides which lack a 2'-OH. Therefore, as stated previously, the specification as filed does not provide sufficient guidance and/or instruction that would allow the skilled artisan to use the ribozymes sequences of the claimed invention, which comprise a DNA sequence, without undue experimentation. This conclusion is based upon the well-established knowledge in the ribozymes art, that

ribozymes are single-stranded RNA molecules, and the lack of guidance provided in the specification as filed for using DNA molecules as ribozymes.

Double Patenting

10. Claims 12-13, 16-21, 25-27, 32-37, 41-52, and 54-77 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/651,754. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application and the instant application are drawn to obvious variants of the same invention, specifically the claims of both applications are drawn to compositions comprising a suppression effector and a replacement nucleic acid that encodes a wild-type or non-disease causing allele and comprises at least one degenerate/wobble nucleotide that is altered so that the replacement nucleic acid is not suppressed or is only partially suppressed by the suppression effector therapeutic compositions for treating a genetic disease. However, the claims of the co-pending application are drawn to compositions comprising a suppression effector that binds to the coding region of a DNA or a mature RNA encoding a mutant allele, wherein said suppression effector inhibits the expression of the mutant allele and a replacement nucleic acid that expresses a wild-type or non-disease causing allele that is not suppressed or is only partially suppressed by the suppression effector. The claims of the current application are drawn to an obvious species of the invention set forth in the copending application. Specifically, the claims of the instant application are drawn to compositions comprising a suppression effector that that suppresses the expression of a mature RNA encoding a mutant allele, and a replacement nucleic acid that encodes a wild-type or non-disease causing allele, and that differs from the mutant allele in at

least one degenerate / wobble nucleotide, and methods of making said suppressor effectors. The claims of the current application and those of the co-pending application differ to the extent that the compositions and methods of the current application are generally drawn to compositions comprising suppression effectors that target the coding region of a mature RNA of a mutant allele, and the claims of the copending application are drawn to compositions and methods comprising suppression effectors that target the coding region of DNA or a mature RNA.

The subject matter as a whole in the instantly claimed invention, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains, over the compositions claimed in the co-pending application since the claims of the instant application represent an obvious species of the invention set forth in the claims of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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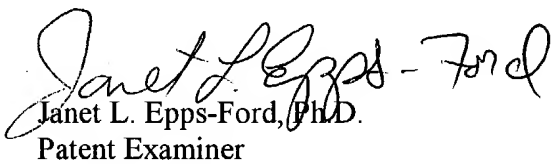

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Patent Examiner
Art Unit 1635

JLE